L3 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:143303 CAPLUS Full-text
DN 140:180238
TI Methods for the isolation and **purification** of ansamitocins
IN Fulston, Mark; Stefanska, Anna L.; Thirkettle, Jan E.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004015119	A2	20040219	WO 2003-US24642	20030807

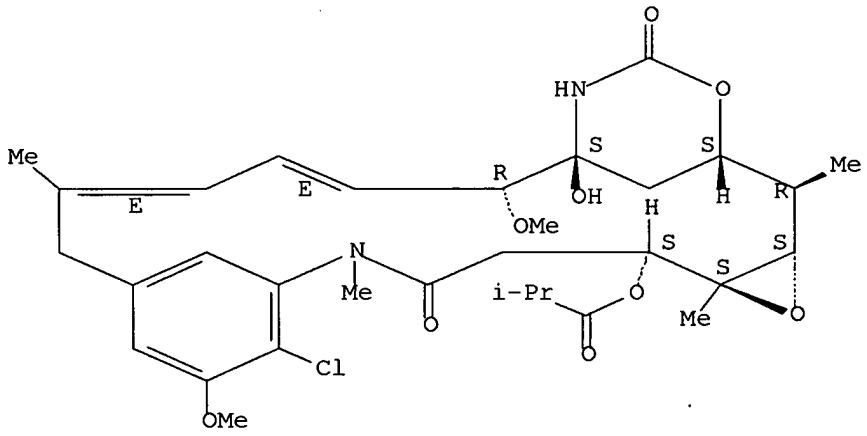
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-401877P P 20020808

AB This invention relates to processes for the preparation of ansamitocins, in particular ansamitocins that can be converted to maytansinol. Thus, 25-26 L of Actinosynnema pretiosum whole fermentation was extracted with toluene broth. The extract was then loaded onto a Biotage flash silica gel chromatog. system. The ansamitocins were eluted with 4% methanol/toluene and the fractions containing ansamitocin P-3 were collected. The eluate fractions were consolidated and evaporated to dryness in a rotary evaporator. The residue slurried in 2 mL methanol followed by 30 mL Et acetate and heated to 50 °C until all the material had dissolved. Prewarmed heptane was then added until clouding began, at which point the flask was allowed to cool to room temperature The recovered crystals consisted of ansamitocin P-3 (86%) along with ansamitocin P-2 (5.7%) and ansamitocin P-4 (7.9%).

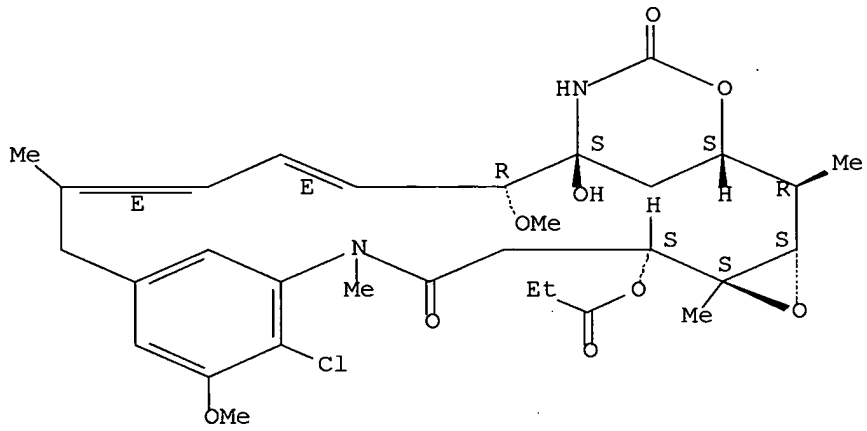
IT **66584-72-3P**, Ansamitocin P-3
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)(methods for isolation and **purification** of ansamitocins)
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



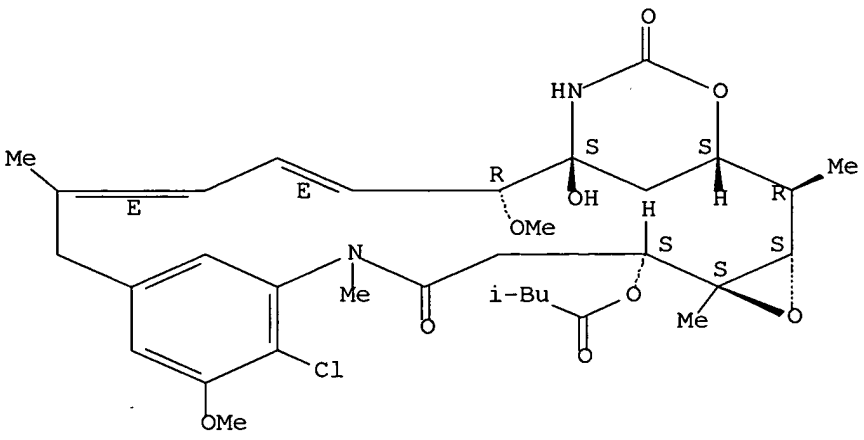
IT **57103-70-5P**, Ansamitocin P-2 **66547-10-2P**, Ansamitocin P-4 RL: BPN (Biosynthetic preparation); BYP (Byproduct); BIOL (Biological study); PREP (Preparation)
(methods for isolation and **purification** of ansamitocins)
RN 57103-70-5 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66547-10-2 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.


O
HN
O
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S
Me
R
OH
H
H
R
Me
E
E
OMe
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N
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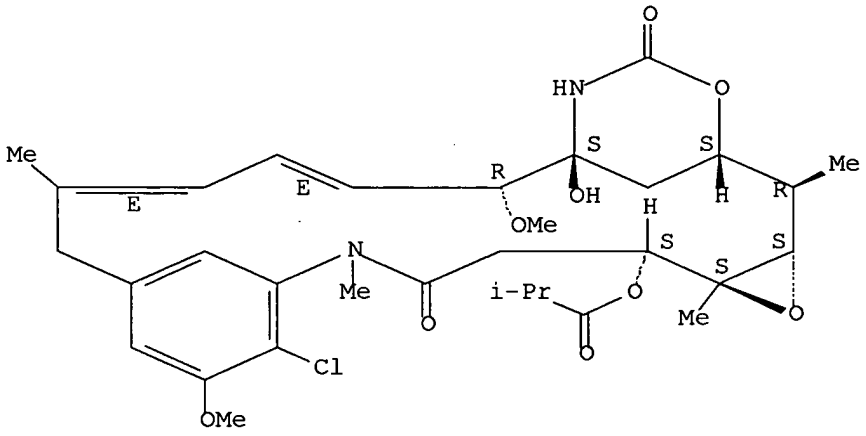
Me
i-Bu
O
Me
O
O
O
Cl
OMe

L3 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:967172 CAPLUS Full-text
DN 140:174510
TI Selective antimicrotubule activity of N1-phenyl-3,5-dinitro-N4,N4-di-n-propylsulfanilamide (GB-II-5) against kinetoplastid parasites
AU Werbovetz, Karl A.; Sackett, Dan L.; Delfin, Dawn; Bhattacharya, Gautam; Salem, Manar; Obrzut, Tomasz; Rattendi, Donna; Bacchi, Cyrus
CS Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH, USA
SO Molecular Pharmacology (2003), 64(6), 1325-1333
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Analogs of the antimitotic herbicide oryzalin (3,5-dinitro-N4,N4-di-n-propylsulfanilamide) were recently prepared that were more potent in vitro than the parent compound against the kinetoplastid parasite Leishmania donovani (Bioorg Med Chem Lett 12:2395-2398, 2002). In the present work, we show that the most active mol. in the group, N1-phenyl-3,5-dinitro- N4,N4-di-n-propylsulfanilamide (GB-II-5), is a potent, selective antimitotic agent against kinetoplastid parasites. GB-II-5 possesses IC50 values of 0.41 and 0.73 μM in vitro against two strains of the related parasite Trypanosoma brucei but is much less toxic to J774 murine macrophages and PC3 prostate cancer cells, exhibiting IC50 values of 29 and 35 μM against these lines, resp. Selectivity is also observed for GB-II-5 with **purified** leishmanial and mammalian tubulin. The assembly of 15 μM leishmanial tubulin is completely inhibited by 10 μM GB-II-5, whereas 40 μM GB-II-5 inhibits the assembly of 15 μM porcine brain tubulin by only 17%. In cultured L. donovani and T. brucei, treatment with 5 and 0.5 μM GB-II-5, resp., causes a striking increase in the fraction of G2M cells compared with control. Given the potency and selectivity of this agent against kinetoplastid tubulin, GB-II-5 emerges as an exciting new antitrypanosomal and antileishmanial lead compound
IT **66584-72-3**, Ansamitocin P3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective antimicrotubule activity of oryzalin analog GB-II-5 against
kinetoplastid parasites)
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:736260 CAPLUS Full-text
DN 137:247554
TI Process for preparation and **purification** of maytansinol
IN Terfloth, Gerald J.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002074775	A1	20020926	WO 2002-US7424	20020312
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002156274	A1	20021024	US 2002-95927	20020311
	EP 1373273	A1	20040102	EP 2002-726608	20020312
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004526734	T2	20040902	JP 2002-573784	20020312
PRAI	US 2001-276792P	P	20010316		
	WO 2002-US7424	W	20020312		

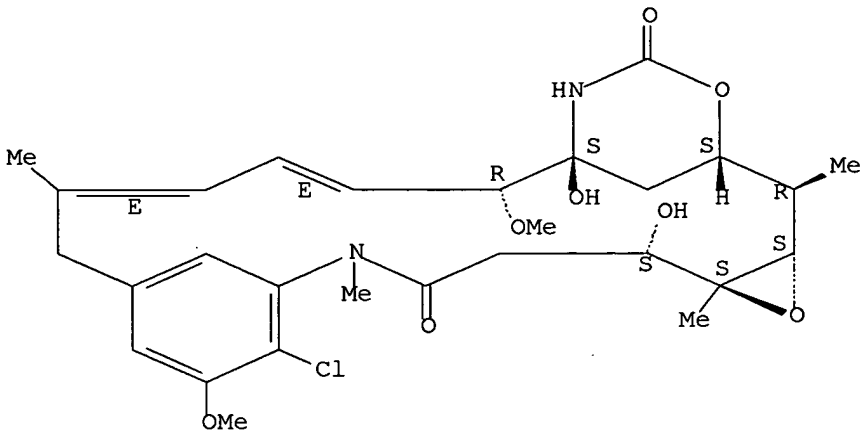
OS CASREACT 137:247554

AB Processes for preparing maytansinol from mixts. containing unreduced and over-reduced maytansinoids by separating the maytansinol by normal-phase high performance liquid chromatog. on a silica, alumina, zirconia, titanium dioxide or chemical modified silica stationary phase. Thus, impure maytansinol prepared by lithium trimethoxyaluminum hydride reduction of ansamitocin P-3 was **purified** by HPLC using a stainless steel column packed with silica gel. to give maytansinol with 99.3% purity. The maytansinol is useful for preparing cell-binding/maytansinoid agent complexes.

IT **57103-68-1P**, Maytansinol
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing and **purification** of maytansinol)

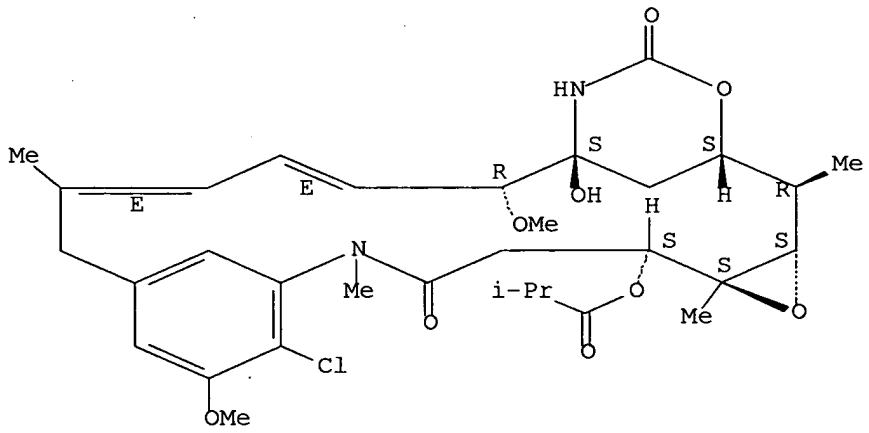
RN 57103-68-1 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **66584-72-3,** Ansamitocin P-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing and **purification** of maytansinol)
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:655114 CAPLUS Full-text
DN 137:201187
TI Process for preparation of cytotoxic conjugates of maytansinoids and cell binding agents
IN Chari, Ravi V. J.; Widdison, Wayne C.
PA Immunogen, Inc., USA
SO U.S., 17 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6441163	B1	20020827	US 2001-867598	20010531
	CA 2417858	AA	20021212	CA 2002-2417858	20020214
	WO 2002098883	A1	20021212	WO 2002-US3378	20020214
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1390370	A1	20040225	EP 2002-720913	20020214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004520450	T2	20040708	JP 2003-502004	20020214
	US 2003055226	A1	20030320	US 2002-161651	20020605
PRAI	US 2001-867598	A	20010531		
	WO 2002-US3378	W	20020214		

OS CASREACT 137:201187; MARPAT 137:201187
GI

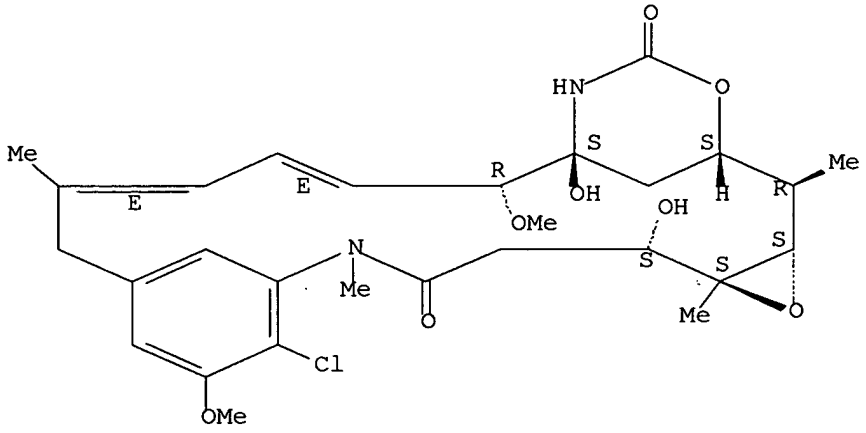
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Maytansinoid derivs. having a disulfide linker, such as I [R1, R2 = H, Me, Et, alkyl; n = 1-5; X = reactive ester], were prepared The reactive ester group of I was reacted with cell binding agents, such as antibodies, to produce conjugates. These conjugates are useful as therapeutic agents which are delivered specifically to target cells and are cytotoxic. Thus, maytansinoid derivative II was prepared via a multistep synthetic sequence starting from 1,3-dibromobutane, sodium cyanide, thiourea, N-hydroxysuccinimide and N2'-deacetyl-N2'-[3-thiopropyl]-maytansine. II was reacted with huN901 antibody and **purified** over a Sephadex gel filtration to provide huN901-maytansinoid conjugate which was potent in killing antigen pos. cells, with an IC50 value of 1x10-10 M.

IT **57103-68-1**, Maytansinol
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of cytotoxic conjugates of maytansinoid derivs.
having a disulfide moiety and huN901 antibody)

RN 57103-68-1 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:934023 CAPLUS Full-text

DN 136:53632

TI Process for the preparation and **purification** of thiol-containing maytansinoids

IN Chari, Ravi Vankeepuram Jagannatha; Widdison, Wayne Charles

PA Immunogen, Inc., USA

SO U.S., 19 pp.
CODEN: USXXAM

DT Patent

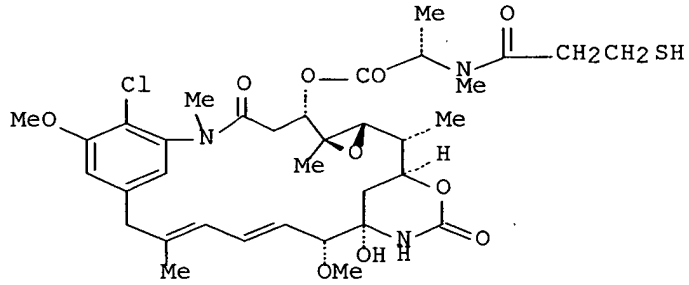
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6333410	B1	20011225	US 2000-641348	20000818
	CA 2373554	AA	20020228	CA 2001-2373554	20010426
	WO 2002016368	A1	20020228	WO 2001-US10816	20010426
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	AU 2001053118	A5	20020304	AU 2001-53118	20010426
	AU 763107	B2	20030710		
	EP 1313738	A1	20030528	EP 2001-926594	20010426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	JP 2004506738	T2	20040304	JP 2002-521468	20010426
PRAI	US 2000-641348	A	20000818		
	WO 2001-US10816	W	20010426		

OS CASREACT 136:53632; MARPAT 136:53632

GI



I

AB The present invention provides a process for the preparation and **purifn**. of thiol-containing maytansinoids comprising the steps of: (1) reductive hydrolysis of a maytansinoid C-3 ester with a reducing agent selected from the group consisting lithium trimethoxyaluminum hydride (LiAl(OMe)3H), lithium triethoxyaluminum hydride (LiAl(OEt)3H), lithium tripropoxyaluminum hydride (LiAl(OPr)3H), sodium trimethoxyaluminum hydride (NaAl(OMe)3H), sodium triethoxyaluminum hydride (NaAl(OEt)3H) and sodium tripropoxyaluminum hydride (NaAl(OPr)3H) to yield a maytansinol; (2) **purifying** the maytansinol to remove side products when present; (3) esterifying the **purified** maytansinol with a carboxylic acid to yield a mixture of an L- and a D-aminoacyl ester of maytansinol; (4) separating the L-aminoacyl ester of maytansinol from the reaction mixture in (3); (5) reducing the L-aminoacyl ester of maytansinol to yield a thiol-containing maytansinoid; and (6) **purifying** the thiol-containing maytansinoid. Thus, ansanmitocin P-3 underwent reductive hydrolysis with LiAl(OMe)3H in THF and the product dissolved in Et

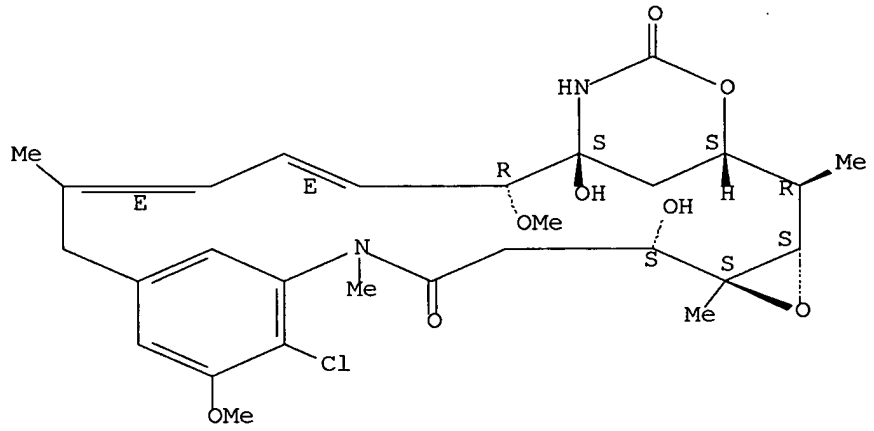
acetate was **purified** on a silica gel column to give pure maytansinol in 71% yield. Maytansinol was treated with N-methyl-N-(3-methyldithiopropanoyl)-L-alanine in CH2Cl2 containing DCC and zinc chloride and the product in MeOH and Et acetate was treated with dithiorheitol in potassium phosphate buffer containing EDTA to give the maytansinoid I.

IT **57103-68-1P**, Maytansinol
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation and **purification** of thiol-containing maytansinoids)

RN 57103-68-1 CAPLUS

CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

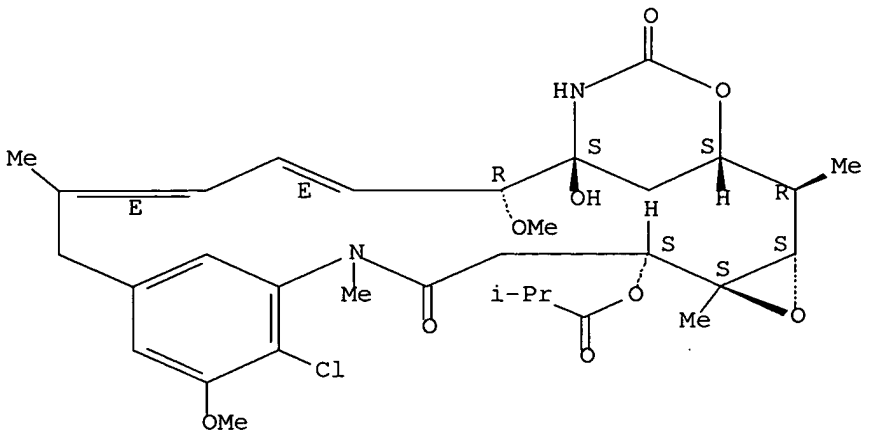


IT **66584-72-3**, Ansamitocin P-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation and **purification** of thiol-containing maytansinoids)

RN 66584-72-3 CAPLUS

CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:763222 CAPLUS Full-text
DN 135:302951
TI Methods for ansamitocin production
IN Fulston, Mark; Stefanska, Anna; Thirkettle, Jan
PA SmithKline Beecham P.L.C., UK
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077360	A2	20011018	WO 2001-GB1661	20010411
	WO 2001077360	A3	20020912		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002015984	A1	20020207	US 2001-828758	20010409
	US 6573074	B2	20030603		
	CA 2406188	AA	20011018	CA 2001-2406188	20010411
	EP 1272653	A2	20030108	EP 2001-966770	20010411
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003530114	T2	20031014	JP 2001-575214	20010411
	BR 2001009975	A	20040323	BR 2001-9975	20010411
	NZ 521868	A	20041126	NZ 2001-521868	20010411
	NO 2002004893	A	20021010	NO 2002-4893	20021010
	ZA 2002008159	A	20031017	ZA 2002-8159	20021010
	US 2003157669	A1	20030821	US 2003-379136	20030304
PRAI	US 2000-196361P	P	20000412		
	US 2001-828758	A3	20010409		
	WO 2001-GB1661	W	20010411		

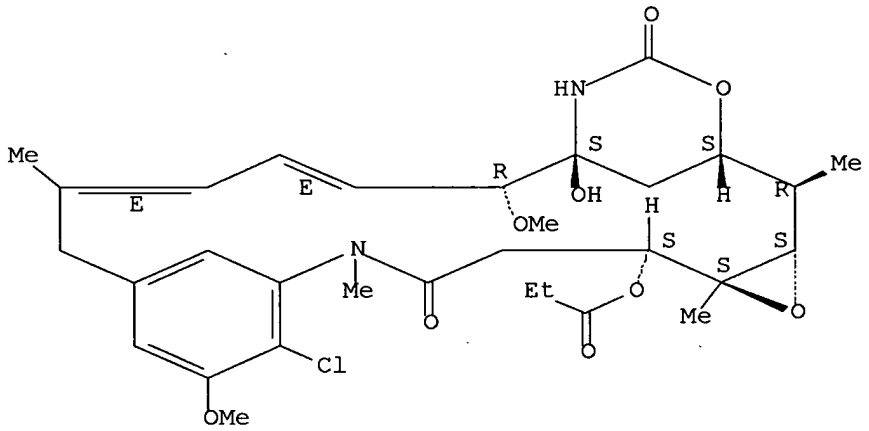
AB Improved **purification** methods for ansamitocins are disclosed. Thus, 37 L of fermentation broth from Actinosynnema pretiosum containing 86.3 mg/L ansamitocin P-3 was heat treated in-situ at 75 °C to kill the microorganisms. Forty L of toluene was added and the mixture was heated to 45°C and agitated for 16 h. After the phases had separated, the toluene layer containing 80 mg/L ansamitocin P-3 was siphoned off and concentrated by evaporation At this point the extract contained 3.1 g of ansamitocin P-3 representing a recovery of ~ 97%. The resulting extract was re-dissolved in toluene and concentrated one again by evaporation This extract was then dissolved in toluene, loaded onto a Kieselgel 60 column, and eluted using a 2% methanol in toluene mobile phase. The ansamitocin P-3 fractions were combined and concentrated yielding an 3.2 g of an oily solid containing 2.5 g of ansamitocin P-3. This solid was taken up in 200 mL Et acetate, warmed to 40 °C, combined with 200 mL heptane and allowed to cool. Once seeded with pure ansamitocin P-3 crystals the crystallization occurred spontaneously. A yield of 2.5 g of crystals was obtained containing 86% (2.15 g)

ansamitocin P-3 with the remainder consisting mostly of other ansamitocins.

IT **57103-70-5P**, Ansamitocin P-2 **66547-09-9P**, Ansamitocin P 3' **66547-10-2P**, Ansamitocin P-4 **66584-72-3P**, Ansamitocin P-3 **72816-08-1P**, Ansamitocin P 4'
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(solvent extraction of ansamitocin from fermentation broth)

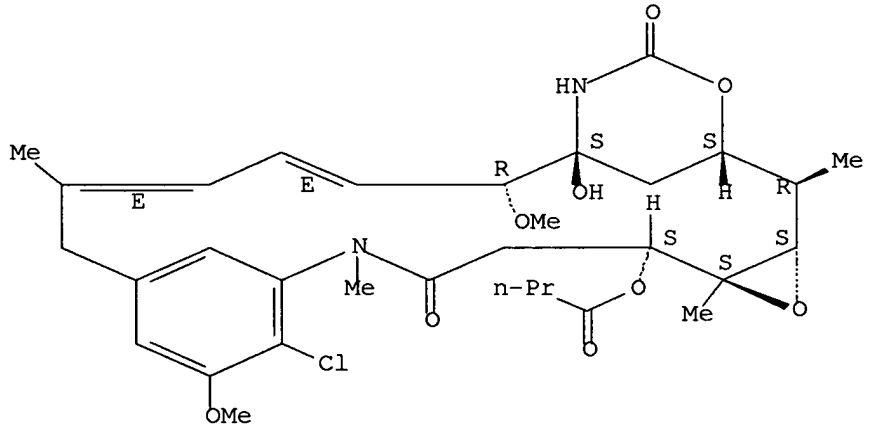
RN 57103-70-5 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



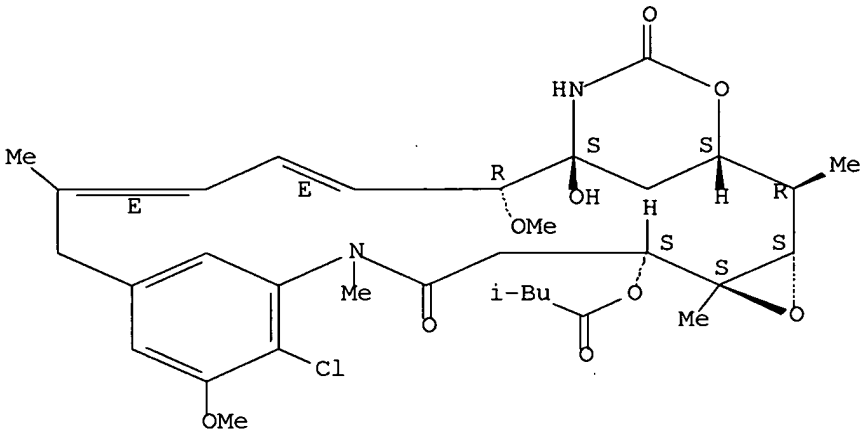
RN 66547-09-9 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



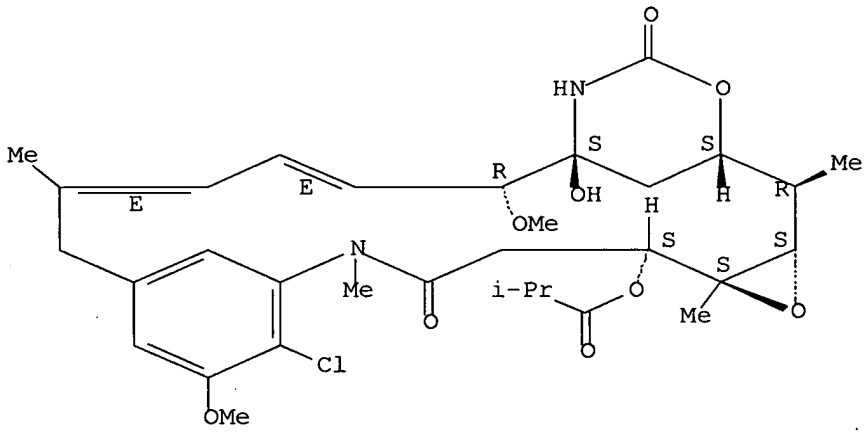
RN 66547-10-2 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



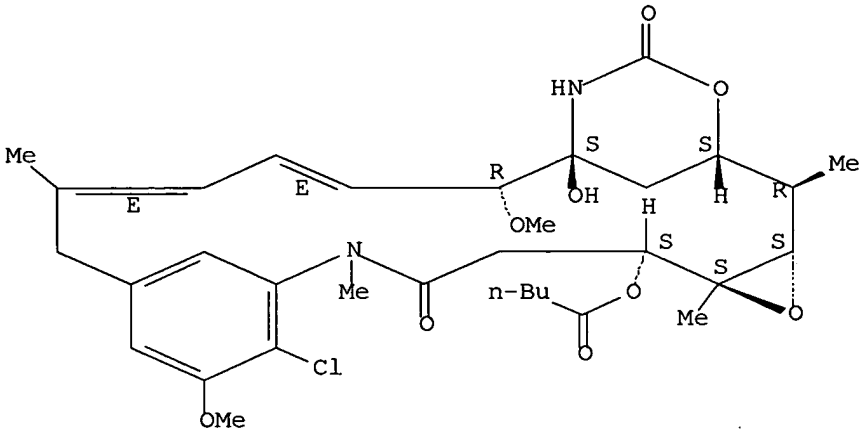
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 72816-08-1 CAPLUS
CN Maytansine, 3-de[2-(acetylmethylamino)-1-oxopropoxy]-3-[(1-oxopentyl)oxy]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.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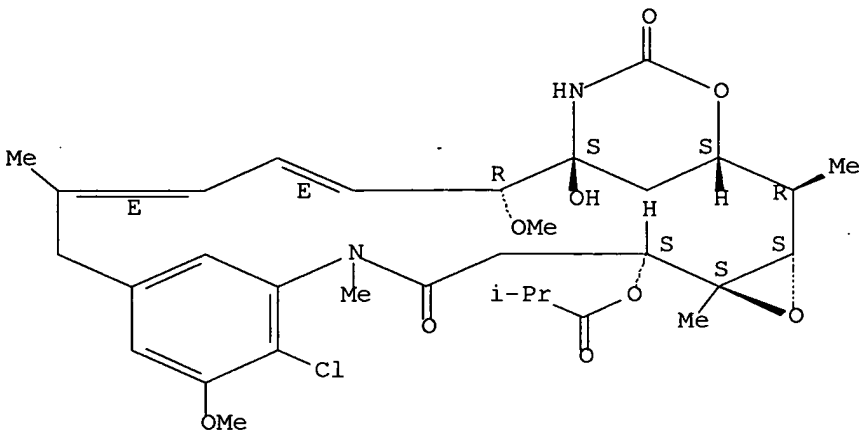
Cl
OMe

L3 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:800767 CAPLUS Full-text
DN 134:51030
TI Cellular effects of leishmanial tubulin inhibitors on L. donovani
AU Havens, Courtney G.; Bryant, Nelva; Asher, Ludmila; Lamoreaux, Laurie; Perfetto, Steve; Brendle, James J.; Werbovetz, Karl A.
CS Department of Parasitology, Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Washington, DC, 20307, USA
SO Molecular and Biochemical Parasitology (2000), 110(2), 223-236
CODEN: MBIPDP; ISSN: 0166-6851
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB To aid our investigation of tubulin as an antileishmanial drug target, the effects of the mammalian antimicrotubule agents ansamitocin P3, taxol, and hemiasterlin on Leishmania donovani promastigotes were described. These drugs affected the assembly of **purified** leishmanial tubulin and inhibited the growth of L. donovani promastigotes at micromolar concns. When promastigotes were treated with these agents, mitotic partitioning of nuclear DNA and cytokinesis were usually inhibited. The spatial orientation of kinetoplasts was often disturbed, suggesting a role for microtubules in the segregation of these organelles during mitosis. Aberrant cell types produced in drug-treated cultures included parasites with one nucleus and two geometrically distinct kinetoplasts, parasites with multiple kinetoplasts, and cytoplasts containing a kinetoplast but no nucleus. A subset of unique cell types, parasites containing two nuclei, a spindle fiber, and two geometrically distinct kinetoplasts, were observed in hemiasterlin-treated cultures. Flow cytometric anal. of L. donovani promastigotes treated with these three drugs indicated a dramatic shift toward the G2 + M phase of the cell cycle, with some cells containing four times the amount of DNA present in G1. These results were used to evaluate the cellular effects of WR85915, an aromatic thiocyanate with in vitro antileishmanial and anti-tubulin activity, on L. donovani. Treatment of parasites with WR85915 did not produce the unusual cell types described above and did not cause the accumulation of parasites in G2 + M, suggesting that WR85915 acts on target(s) in Leishmania in addition to tubulin. These studies validate tubulin as a suitable antileishmanial drug target and provide criteria to assess the cellular mechanism of action of new candidate antileishmanial agents.
IT **66584-72-3**, Ansamitocin P3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cellular effects of leishmanial tubulin inhibitors on L. donovani)
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

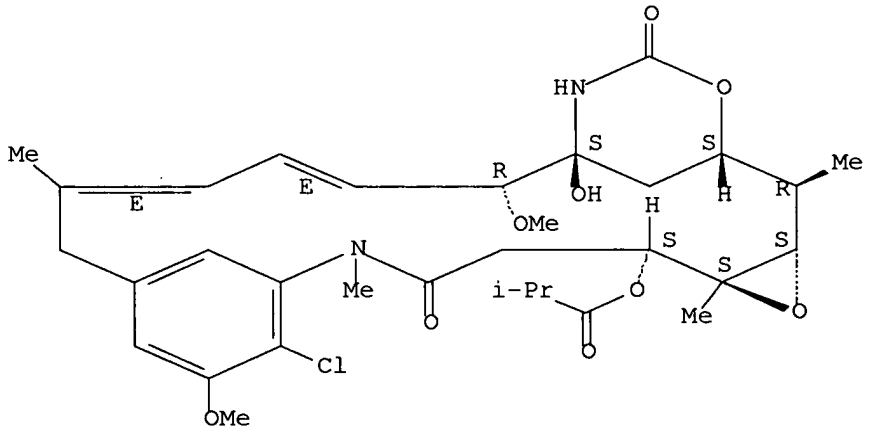
Absolute stereochemistry.
Double bond geometry as shown.



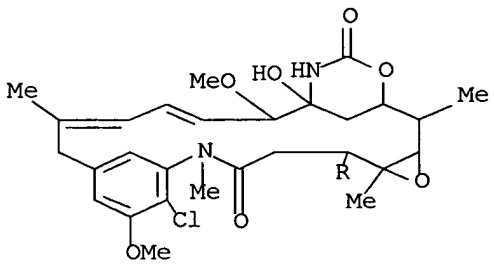
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

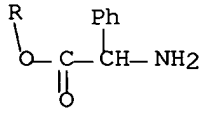
L3 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:625828 CAPLUS Full-text
DN 117:225828
TI Therapeutic effect of ansamitocin targeted to tumor by a bispecific monoclonal antibody
AU Okamoto, Kayoko; Harada, Kaori; Ikeyama, Shuichi; Iwasa, Susumu
CS Biol. Res. Lab., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SO Japanese Journal of Cancer Research (1992), 83(7), 761-8
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
AB The authors have constructed a murine hybrid hybridoma that secretes a bispecific monoclonal antibody (mAb) by fusing a hybridoma secreting an anti-ansamitocins mAb with a hybridoma secreting an anti-human transferrin receptor (TfR) mAb that binds to human A431 epidermoid carcinoma cells. The bispecific mAb, reactive to both ansamitocins and TfR, was **purified** by a combination of hydrophobic column chromatog. and hydroxyapatite high-performance liquid chromatog., and evaluated in in vivo expts. using human tumor cell-implanted nude mice. Ansamitocin P-3 targeted through one of the antigen combining sites of the bispecific mAb was potentially more effective in suppressing the growth of estimated A431 tumor xenografts implanted on nude mice than unconjugated ansamitocin P-3 or the immunoconjugate of ansamitocin P-3 and monospecific antiansamitocins antibody, and the targeted ansamitocin P-3 finally eradicated the tumor mass. The bispecific mAb also played an important role in reducing such undesirable side-effects of ansamitocin P-3 as the loss of body weight, the damage to liver functions and the decrease in the number of white blood cells.
IT **66584-72-3D**, Ansamitocin P-3, monoclonal antibody conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bispecific to ansamitocin and transferrin receptor, antitumor activity of)
RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **133319-65-0P**, TAC 582
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conjugation with bispecific monoclonal antibody to ansamitocin and transferrin receptor of)
RN 133319-65-0 CAPLUS
CN Maytansine, O3-(aminophenylacetyl)-O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

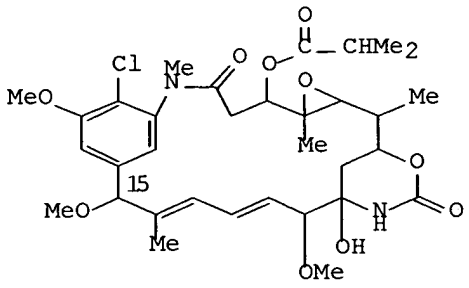




L3 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:179511 CAPLUS Full-text
DN 110:179511
TI Isolation of maytansinoid compound as an antitumor agent
IN Sakai, Kunikazu; Yamada, Kaoru; Ichikawa, Tetsuya; Yamashita, Mitsuo; Kondo, Sei
PA Sagami Chemical Research Center, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63233986	A2	19880929	JP 1987-65657	19870323
PRAI	JP 1987-65657		19870323		

GI



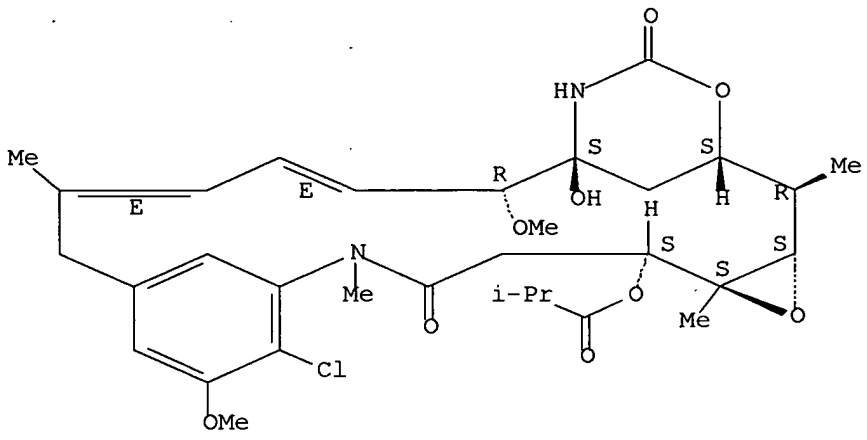
I

AB Maytansinoid compound I, an effective antitumor agent, is isolated from Isothecium subdiversiforme. Isothecium subdiversiforme (14.5 kg) was frozen with liquid N, crushed, extracted with Et2O, the exts. concentrated in vacuo to give a crude mixture, which was **purified** by adsorption, desorption, and chromatographed to give I, which showed IC50 of 1 + 10-5 to 3 + 10-4 μg/mL against P-388 leukemia cells.

IT **66584-72-3**
RL: PROC (Process)
(isolation of, as antitumor agent)

RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.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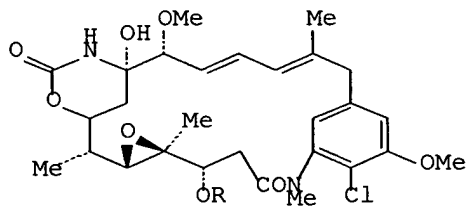
OMe

L3 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:508519 CAPLUS Full-text
DN 97:108519
TI Antibiotic C-15003
IN Higashide, Eiji; Asai, Mitsuko; Tanida, Seiichi
PA Takeda Chemical Industries, Ltd. , Japan
SO Can., 32 pp. Division of Can. Appl. No. 288,731.
CODEN: CAXXA4
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 1121814	A2	19820413	CA 1981-373582	19810320
	JP 53130693	A2	19781114	JP 1977-37166	19770331
	JP 60034556	B4	19850809		
	US 4162940	A	19790731	US 1977-811448	19770629
	FR 2385714	A1	19781027	FR 1977-30339	19771007
	FR 2385714	B1	19820514		
	SU 741804	D	19800615	SU 1977-2529301	19771007
	HU 28459	O	19831228	HU 1981-2440	19771013
	HU 187372	B	19851228		
	AT 7707362	A	19810215	AT 1977-7362	19771014
	AT 364081	B	19810925		
	CA 1107212	A1	19810818	CA 1977-288731	19771014
	PL 122289	B1	19820731	PL 1977-201541	19771015
	CH 637137	A	19830715	CH 1977-12605	19780101
	BE 865589	A1	19781002	BE 1978-186486	19780331
	BE 865590	A1	19781002	BE 1978-186487	19780331
	ZA 7801862	A	19790328	ZA 1978-1862	19780331
	ZA 7801863	A	19790328	ZA 1978-1863	19780331
	SU 890978	A3	19811215	SU 1978-2627804	19780620
	AT 7808226	A	19800915	AT 1978-8226	19781117
	AT 362061	B	19810427		
	DK 8003388	A	19800806	DK 1980-3388	19800806
	DK 148180	B	19850422		
PRAI	JP 1977-37166	A	19770331		
	US 1977-811448	A	19770629		
	CA 1977-288731	A3	19771014		
	JP 1977-37886	A	19770401		
	US 1977-811449	A	19770629		
	AT 1977-7362	A	19771014		
	DK 1977-4588	A	19771014		

GI



I

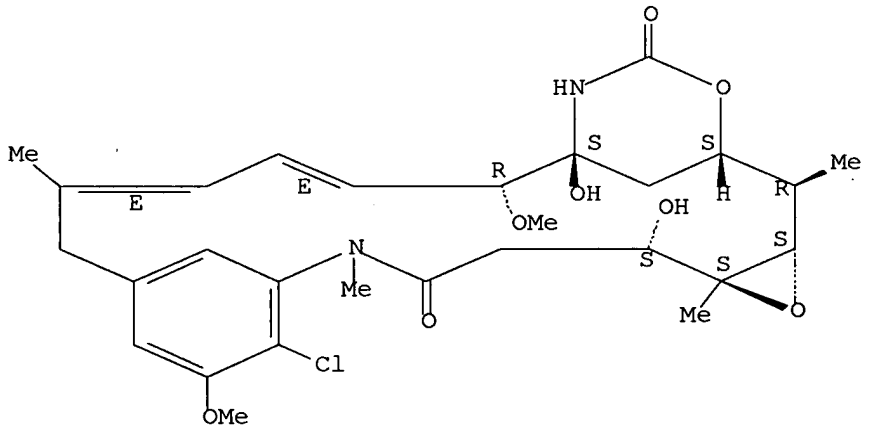
AB Antibiotic C-15003 (I) and its derivs. C-15003 P-ϕ (I;R=H) [**57103-68-1**], C-15003 P-3 (I; R = -COCH(CH3)2), C-15003 P-4 (I; R = -COCH2CH(CH3)2, and C-15003 P-3' (I; R = -CO(CH2)2CH3) are isolated from the actinomycete Nocardia strain C-15003. I was active against gram-

pos. and gram-neg. bacteria, fungi, and leukemia P388, while its LD50 was 0.313 mg/kg. Thus, Nocardia Number C-15003 (ATCC31281) was used to prepare a seed culture which was then inoculated into a nutrient medium (pH 7.0) comprising dextrin 5, corn steep liquor 3, polypeptone 0.1, and CaCO3 0.5%. After incubation for 90 h at 28°, 10 parts of the inoculum was transferred to 2000 parts by volume of a fermentation medium similar to the above and incubated for 48 h 28°. Five hundred parts of this culture was in turn transferred to 30,000 parts by volume of a nutrient medium as described above before final inoculation of 100,000 parts production medium with the seed culture and incubation for 90 h at 28° with aeration. After filtration of the culture broth, the filtrate was extracted with EtOAc and washed with H2O, and then dried and conductivity under vacuum. Addition of petroleum ether to the concentrate gave I as a crude precipitate that was dissolved in EtOAc and the filtrate concentrated under reduced pressure. Further **purification** and fractionation on Diaion HP-10 yielded C-15003 P-3, P-3', and P-4.

IT **57103-68-1 66547-09-9 66547-10-2 66584-72-3**
RL: BIOL (Biological study)
(Nocardia)

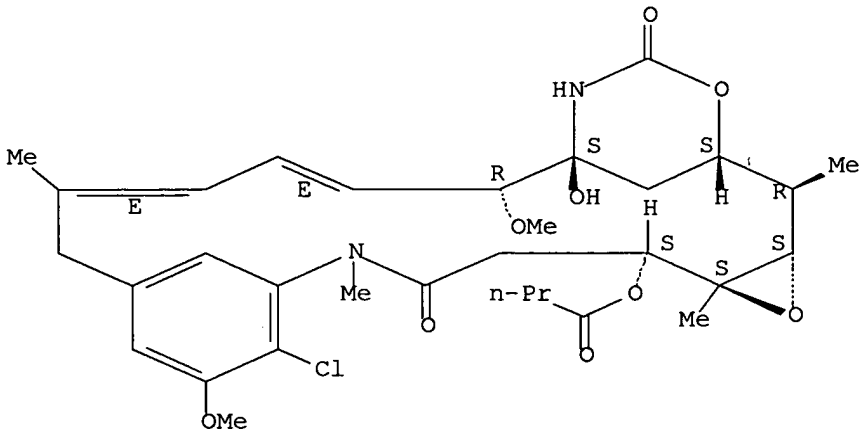
RN 57103-68-1 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



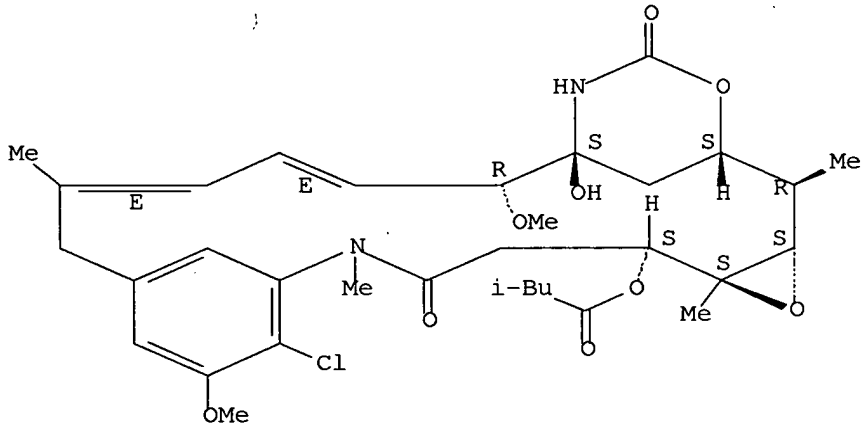
RN 66547-09-9 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



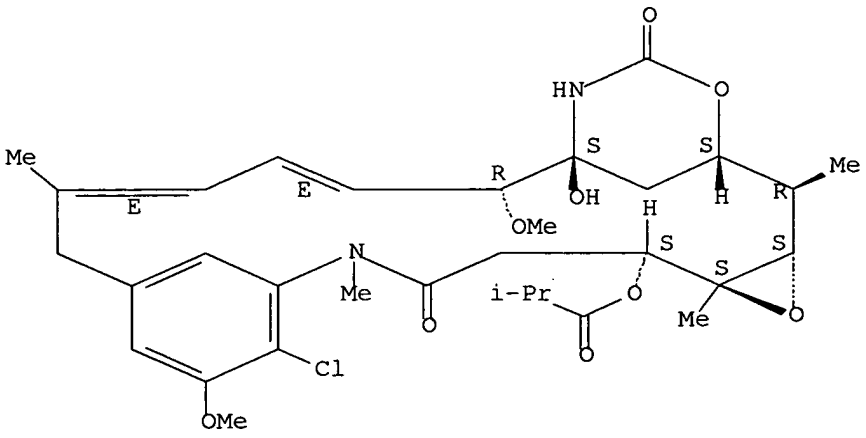
RN 66547-10-2 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.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OMe

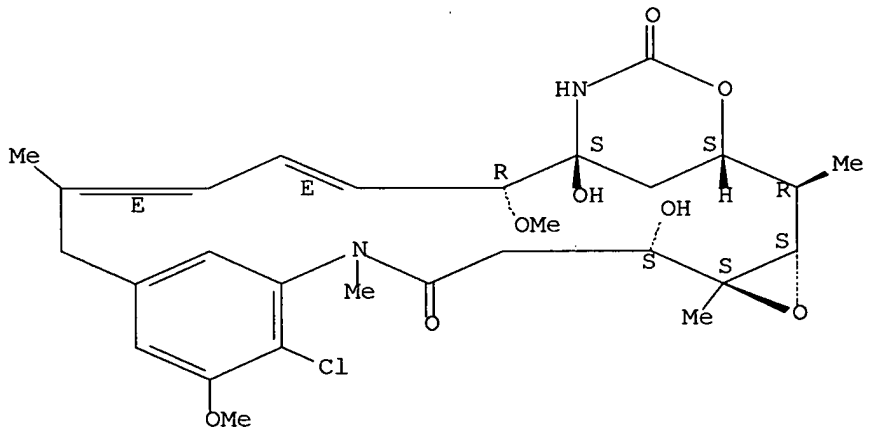
L3 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:468699 CAPLUS Full-text
DN 93:68699
TI Maytansinol
PA Takeda Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 55029972	A2	19800303	JP 1978-103547	19780824
PRAI JP 1978-103547		19780824		

AB Maytansinol (I) [**57103-68-1**] is produced from maytanacine, maytansinol propionate, or ansamitocins, catalyzed by the culture broth or an enzyme preparation of Streptomyces. Thus, S. coelicolor ATCC 13405 was cultured with shaking at 28° for 48 h on 10 L medium (pH 7.5) containing dextrin 2, peptone 0.5, yeast extract 0.5, and meat extract 0.5%. The broth was mixed with 500 mg ansamitocin P-4 [**66547-10-2**] and reacted with shaking at 28° for 24 h to yield I. The reaction mixture was extracted with EtOAc. The extract was washed with 0.005N HCl, 0.5% NaHCO3, and H2O, dried with Na2SO4, and concentrated under vacuum. The concentrate was mixed with petroleum ether to precipitate 1.87 g crude I. **Purification** was by silica gel column and thin layer chromatog. with crystallization from EtOAc, giving a yield of 381 mg.

IT **57103-68-1P**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Stryptomyces)
RN 57103-68-1 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



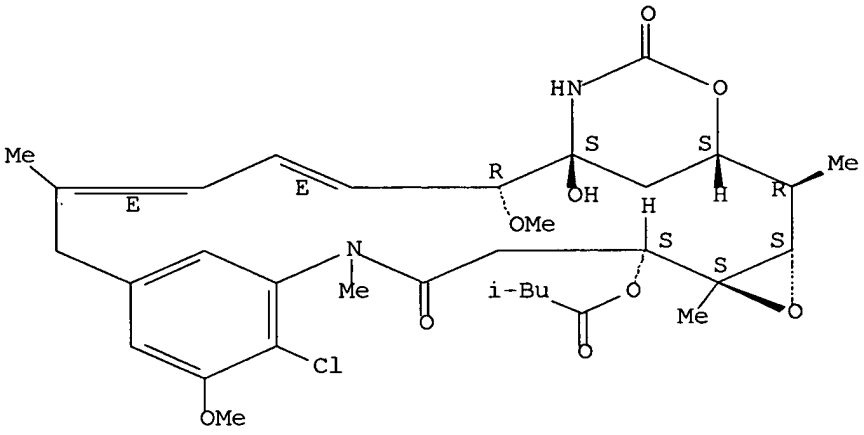
IT **66547-10-2**

RL: BIOL (Biological study)
(maytansinol manufacture from, with Stryptomyces)

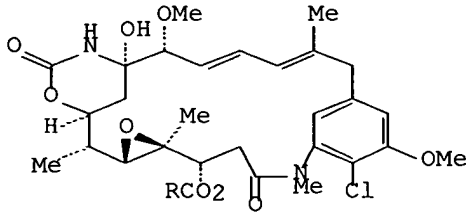
RN 66547-10-2 CAPLUS

CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:179027 CAPLUS Full-text
DN 92:179027
TI Ansamitocins, maytansinoid antitumor antibiotics. Producing organism, fermentation, and antimicrobial activities
AU Tanida, Seiichi; Hasegawa, Toru; Hatano, Kazunori; Higashide, Eiji; Yoneda, Masahiko
CS Microbiol. Res. Lab., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SO Journal of Antibiotics (1980), 33(2), 192-8
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



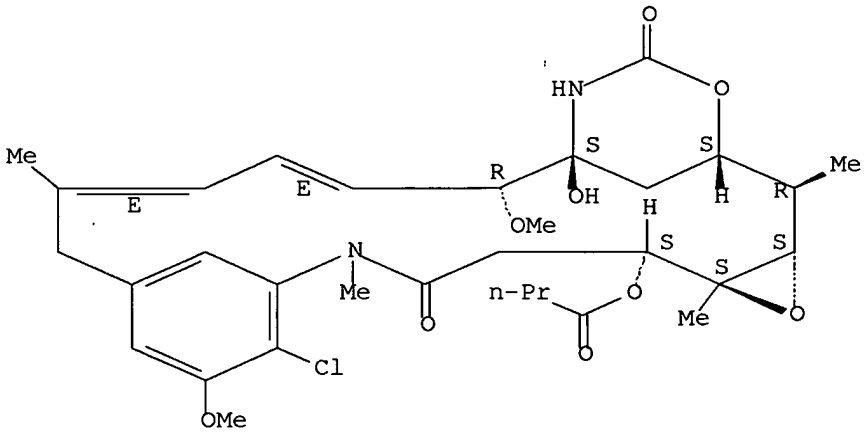
I, R=CHMe2
II, R=Pr
III, R=CH2CHMe2

AB Ansamitocins are new maytansinoid antitumor antibiotics produced by an actinomycete strain Number C-15003 (N-1). The organism was designated Nocardia sp. C-15003 (N-1). In the fermentation fluids, activity against eukaryotic microorganisms was detected. Three of the **purified** materials, which have the activity against Tetrahymena pyriformis strain W and Hamigera avellanea IFO 7721, were new ansamycin antibiotics with antileukemic activities and were named ansamitocins P-3 (I) [**66584-72-3**], P-3' (II) [**66547-09-9**], and P-4 (III) [**66547-10-2**]. Ansamitocins show growth inhibitory activity against several eukaryotic microorganisms but no activity against prokaryotic microorganisms. The acyl moieties at the C-3 position of ansamitocins are essential for their antifungal activities.

IT **66547-09-9 66547-10-2 66584-72-3**
RL: BIOL (Biological study)
(antibiotic, from Nocardia)

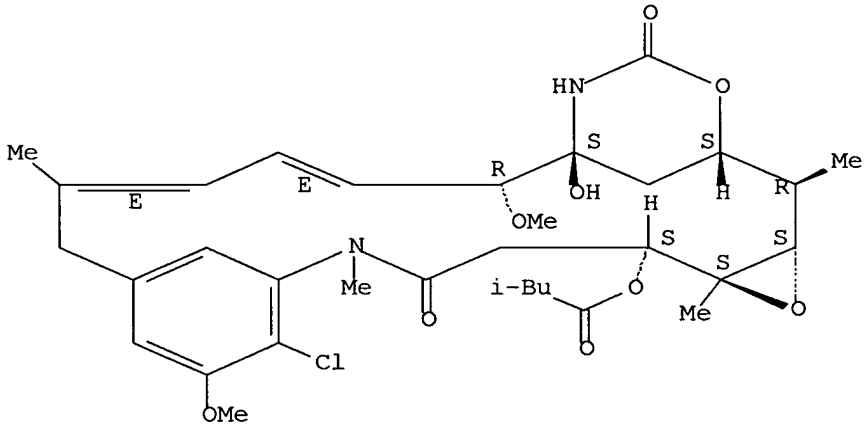
RN 66547-09-9 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



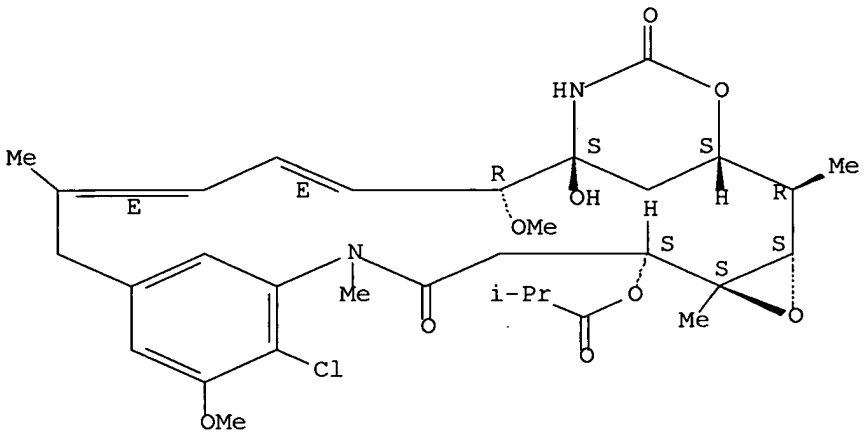
RN 66547-10-2 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

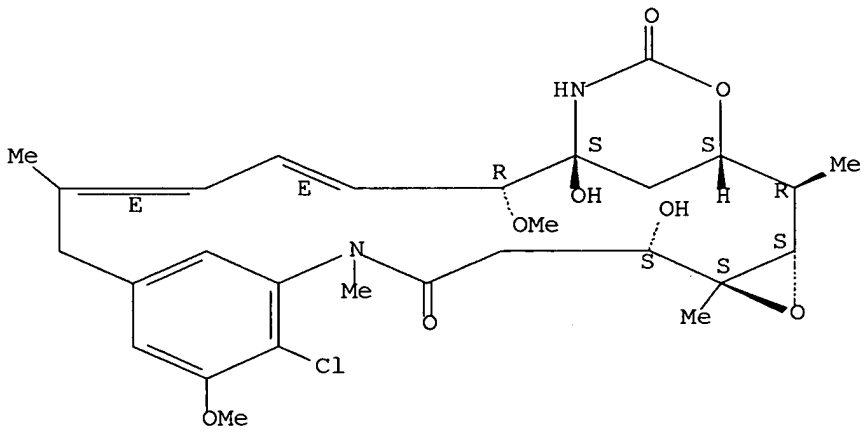


IT **57103-68-1 57103-70-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (fungicidal activity of)

RN 57103-68-1 CAPLUS

CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

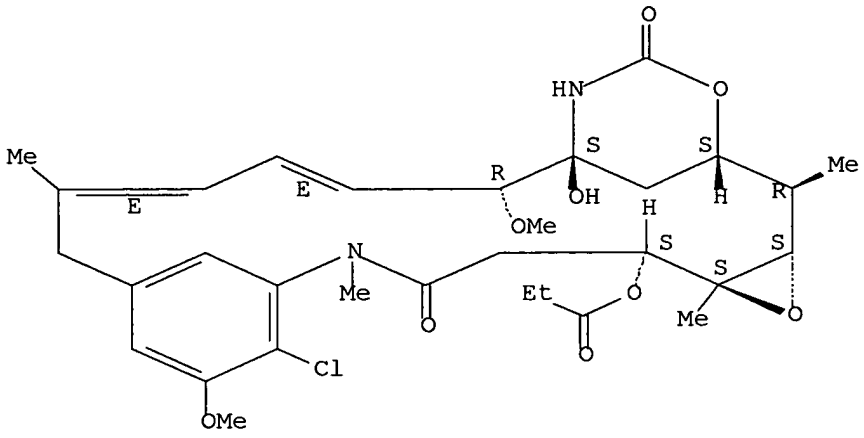
Absolute stereochemistry.
Double bond geometry as shown.



RN 57103-70-5 CAPLUS

CN Maytansine, 2'-de(acetylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.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L3 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:4697 CAPLUS Full-text
DN 92:4697
TI Antibiotic C-15003P-2
IN Higashide, Eiji; Hatano, Kazunori; Asai, Mitsuko
PA Takeda Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 54076895	A2	19790619	JP 1977-141837	19771125
	JP 60016237	B4	19850424		
PRAI	JP 1977-141837		19771125		

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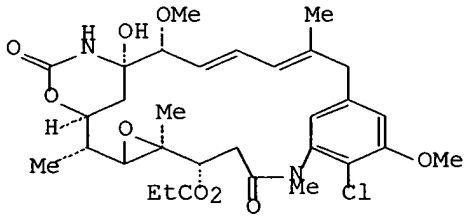
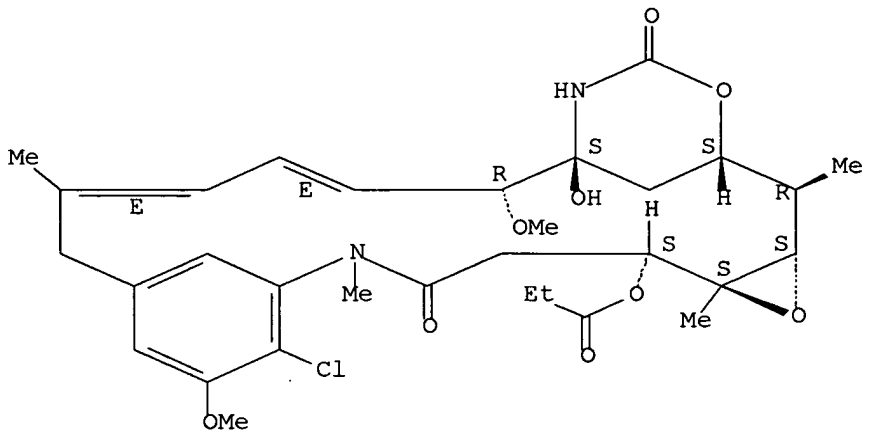


I

AB Antibiotic C-15003P-2 (I) [**57103-70-5**] was produced by culturing a Nocardia species on a medium containing a precursor of PrO·CoA, propionic acid, leucine analog, or valine analog. Thus, Nocardia C-15003 (FERM-P 0992) was aerobically cultured at 28° for 8 days on 100 L of a medium containing soluble starch 3, NH4Cl 0.2, MgSO4 0.05, KH2PO4 1.09, K2HPO4 2.09, FeSO4 0.001, and Na propionate 0.05%. Production of I was 2.0 μg/mL. The culture broth was mixed with 50 L acetone and filtered. The filtrate (135 L) was mixed with water 50 and EtOAc 90 L. The EtOAc layer was washed with water and dried with Na2SO4 and I was precipitated with addition of petroleum ether. The precipitate (15 g) was **purified** by silica gel column chromatog. and crystallized from EtOAc with a yield of 180 mg. It was further **purified** by a column chromatog. on Diaion HP-10.

IT **57103-70-5**
RL: BIOL (Biological study)
(antibiotic, from Nocardia)
RN 57103-70-5 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.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L3 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1979:136271 CAPLUS Full-text
DN 90:136271
TI Maytansinol, maytansine, and maytansinol propionate
IN Higashide, Eiji; Asai, Mitsuko; Tanida, Seiichi
PA Takeda Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

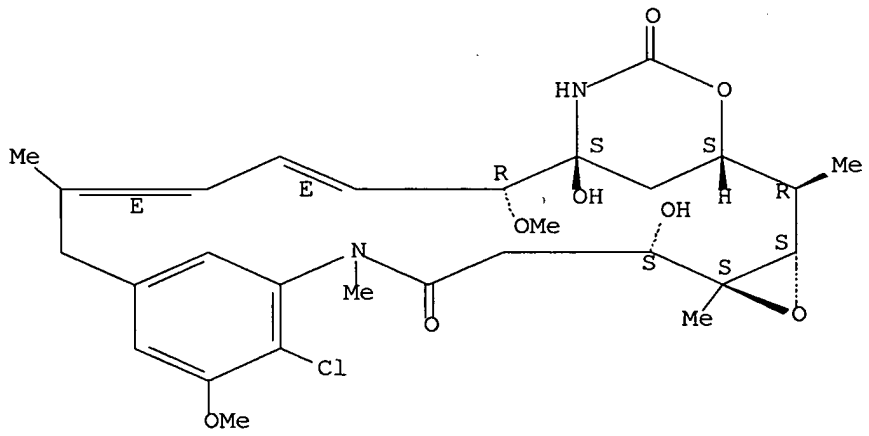
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 53124692	A2	19781031	JP 1977-37885	19770401
	US 4151042	A	19790424	US 1977-811442	19770629
PRAI	JP 1977-37167		19770331		
	JP 1977-37885		19770401		

AB Maytansinol (I) [**57103-68-1**], maytansine (II) [35846-53-8] and maytansinol propionate (III) [**57103-70-5**] were produced by a Nocardia. Thus, Nocardia Number C-15003 (FERM-P 3992) was aerobically cultured at 28° for 90 h on a medium (pH 7.0) containing dextrin 5, corn steep liquor 2, peptone 0.1, and CaCO3 0.5%. The culture filtrate (85 L) was extracted with EtOAc, the extract dried and concentrated in vacuo, and the concentrate mixed with petroleum ether to yield 53 g precipitate The precipitate was dissolved in EtOAc and subjected to column chromatog. on silica gel, eluting with a mixture of hexane and EtOAc to sep. 2 g I and crude mixture The crude mixture was **purified** by silica gel chromatog., eluting with a mixture of CHCl3 and MeOH to yield 50 mg mixture of II and III, which were separated by column. chromatog. on Diaion HP-10, yielding 13 mg II and 25 mg III.

IT **57103-68-1P 57103-70-5P**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Nocardia)

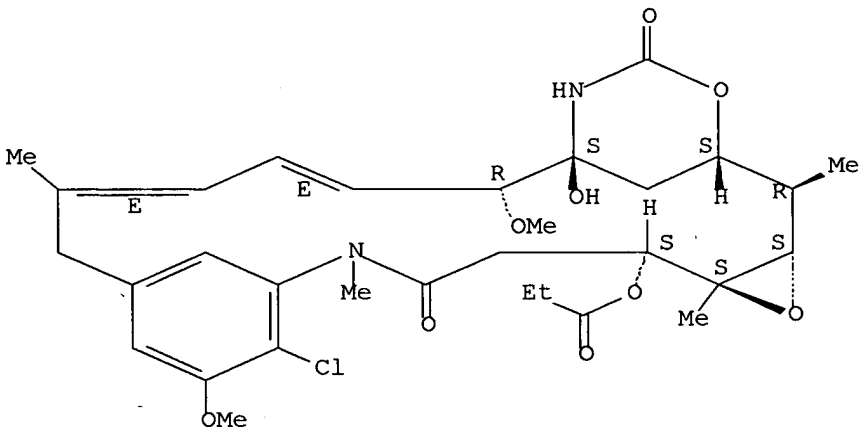
RN 57103-68-1 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 57103-70-5 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1979:53132 CAPLUS Full-text
DN 90:53132
TI Antibiotic C-15003
IN Higashide, Eiji; Asai, Mitsuko; Tanida, Seiichi
PA Takeda Chemical Industries, Ltd., Japan
SO Ger. Offen., 51 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2746209	A1	19781019	DE 1977-2746209	19771014
	DE 2746209	C2	19901031		
	JP 53130693	A2	19781114	JP 1977-37166	19770331
	JP 60034556	B4	19850809		
	US 4162940	A	19790731	US 1977-811448	19770629
	FR 2385714	A1	19781027	FR 1977-30339	19771007
	FR 2385714	B1	19820514		
	SU 741804	D	19800615	SU 1977-2529301	19771007
	SE 7711542	A	19781001	SE 1977-11542	19771013
	SE 442873	B	19860203		
	SE 442873	C	19860522		
	NL 7711274	A	19781003	NL 1977-11274	19771013
	NL 188102	B	19911101		
	NL 188102	C	19920401		
	HU 20618	O	19810828	HU 1977-TA1459	19771013
	HU 178359	P	19820428		
	CS 214749	P	19820528	CS 1977-6678	19771013
	HU 28459	O	19831228	HU 1981-2440	19771013
	HU 187372	B	19851228		
	DK 7704588	A	19781001	DK 1977-4588	19771014
	ES 463207	A1	19790101	ES 1977-463207	19771014
	AT 7707362	A	19810215	AT 1977-7362	19771014
	AT 364081	B	19810925		
	GB 1586688	A	19810325	GB 1977-42822	19771014
	PL 122289	B1	19820731	PL 1977-201541	19771015
	PL 124349	B1	19830131	PL 1977-221358	19771015
	CH 637137	A	19830715	CH 1977-12605	19780101
	BE 865589	A1	19781002	BE 1978-186486	19780331
	BE 865590	A1	19781002	BE 1978-186487	19780331
	ZA 7801862	A	19790328	ZA 1978-1862	19780331
	ZA 7801863	A	19790328	ZA 1978-1863	19780331
	SU 890978	A3	19811215	SU 1978-2627804	19780620
	ES 472230	A1	19790401	ES 1978-472230	19780731
	AT 7808226	A	19800915	AT 1978-8226	19781117
	AT 362061	B	19810427		
	DK 8003388	A	19800806	DK 1980-3388	19800806
	DK 148180	B	19850422		
	SE 8302517	A	19830503	SE 1983-2517	19830503
	SE 446004	B	19860804		
	SE 446004	C	19861113		
PRAI	JP 1977-37166	A	19770331		
	US 1977-811448	A	19770629		
	JP 1977-37886	A	19770401		
	US 1977-811449	A	19770629		

	AT 1977-7362	A	19771014
	DK 1977-4588	A	19771014

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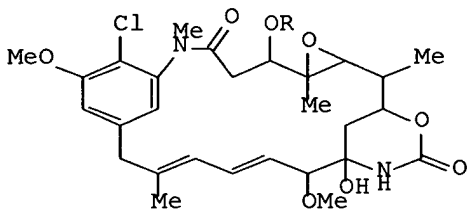


I, R=COCHMe2
II, R=COPr
III, R=COCH2CHMe2

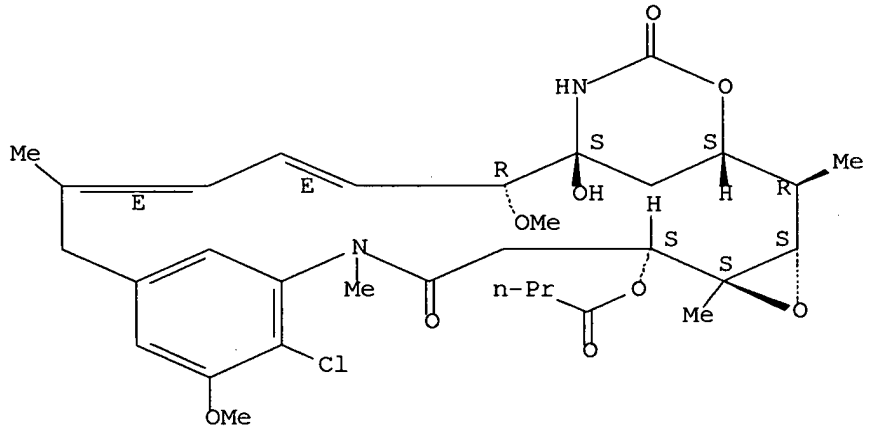
AB Antibiotics C-15003 P-3 (I) [**66584-72-3**], C-15003 P-3' (II) [**66547-09-9**], and C-15003 P-4 (III) [**66547-10-2**] are produced by fermentation with Nocardia C-15003 (ATCC 31281). Thus, a preculture of Nocardia was inoculated into a pH 7 medium containing dextrin 5, corn steep liquor 3, polypeptone 0.1, and CaCO3 0.5% and incubated at 28° for 90 h. The titer at this time was 25 μg C-15003/mL. C-15003 was **purified** by extraction into EtOAc, precipitation from petroleum ether, and chromatog. on silica gel. I, II, and III were separated by chromatog. on Diaion HP-10 with aqueous MeOH and NaCl. C-15003 had fungicidal and leukemia-inhibiting properties.

IT **66547-09-9 66547-10-2 66584-72-3**
RL: BIOL (Biological study)
(from Nocardia)

RN 66547-09-9 CAPLUS

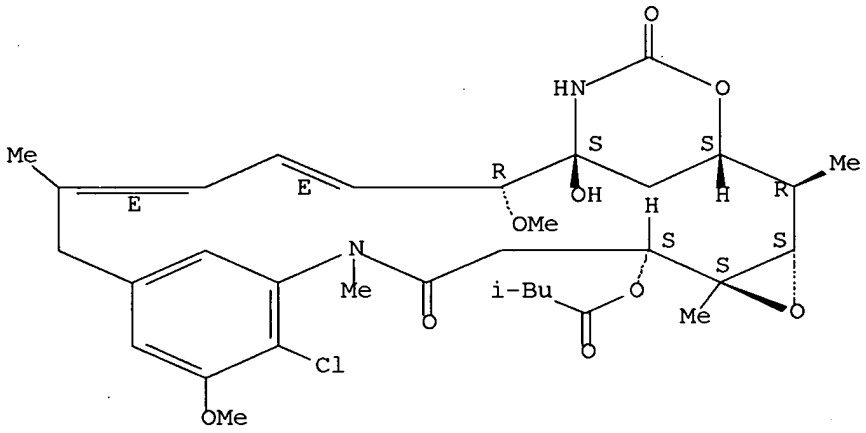
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(1-oxobutyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



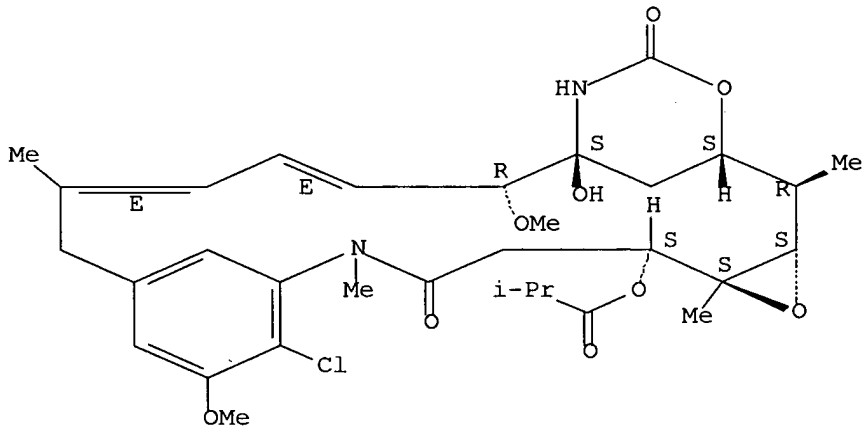
RN 66547-10-2 CAPLUS
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1979:34105 CAPLUS Full-text
DN 90:34105
TI Composition containing antibiotic C-15003 for treating tumors in warm-blooded animals
IN Higashide, Eiji; Asai, Mitsuko; Tanida, Seiichi; Otsu, Koichiro; Kozai, Yoshio
PA Takeda Chemical Industries, Ltd., Japan
SO Ger. Offen., 53 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2746252	A1	19781005	DE 1977-2746252	19771014
	JP 53130693	A2	19781114	JP 1977-37166	19770331
	JP 60034556	B4	19850809		
	JP 54014511	A2	19790202	JP 1977-113131	19770919
	AU 510499	B2	19800626	AU 1977-29074	19770923
	AU 7729074	A1	19790329		
	FR 2385714	A1	19781027	FR 1977-30339	19771007
	FR 2385714	B1	19820514		
	SU 741804	D	19800615	SU 1977-2529301	19771007
	NL 7711272	A	19781003	NL 1977-11272	19771013
	HU 28459	O	19831228	HU 1981-2440	19771013
	HU 187372	B	19851228		
	AT 7707362	A	19810215	AT 1977-7362	19771014
	AT 364081	B	19810925		
	GB 1592264	A	19810701	GB 1977-42823	19771014
	PL 122289	B1	19820731	PL 1977-201541	19771015
	CH 637137	A	19830715	CH 1977-12605	19780101
	BE 865589	A1	19781002	BE 1978-186486	19780331
	BE 865590	A1	19781002	BE 1978-186487	19780331
	ZA 7801862	A	19790328	ZA 1978-1862	19780331
	ZA 7801863	A	19790328	ZA 1978-1863	19780331
	SU 890978	A3	19811215	SU 1978-2627804	19780620
	AT 7808226	A	19800915	AT 1978-8226	19781117
	AT 362061	B	19810427		
	DK 8003388	A	19800806	DK 1980-3388	19800806
	DK 148180	B	19850422		
PRAI	JP 1977-37166	A	19770331		
	US 1977-811449	A	19770629		
	US 1977-811448	A	19770629		
	AT 1977-7362	A	19771014		
	DK 1977-4588	A	19771014		

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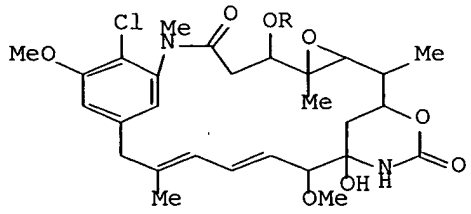


I, R=COCHMe2
II, R=COPr
III, R=COCH2CHMe2

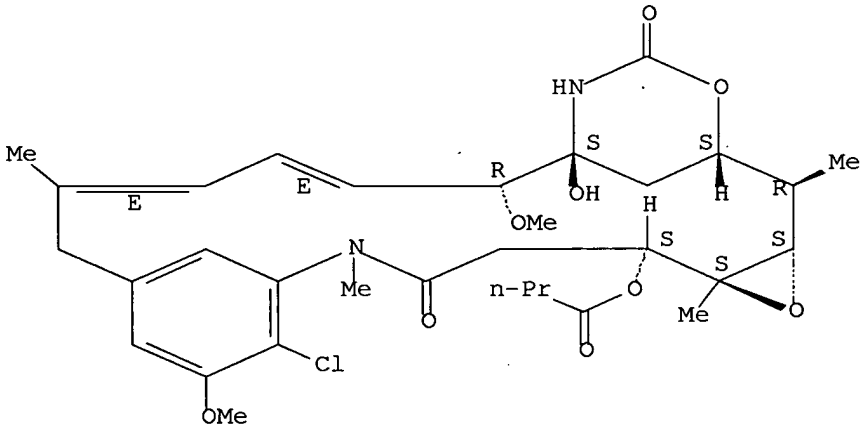
AB Antibiotic C-15003 P-3 (I) [**66584-72-3**], Antibiotic C-]5003 P-3' (II) [**66547-09-9**], and Antibiotic C-15003 P-4 (III) [**66547-10-2**], or mixts. thereof, possess antitumor properties. I, m.p. 190-2°, [α]D22 -136° (c 0.375, CHCl3), II, m.p. 182-5°, [α]D22 -134° (c 0.11, CHCl3), and III, m.p. 177-80°, [α]D22 -142° (c 0.522, CHCl3) are **purified** from the fermentation products of Nocardia new species strain C-15003. Thus, treatment with I, II, and III or their mixts. prolonged the survival time of mice bearing leukemia P388, melanoma B16, leukemia L1210, sarcoma 180, Ehrlich carcinoma, and mastocytoma P815. The fermentative production and **purification** of the 3 compds. are described as well as their spectral properties leading to structure elucidation.

IT **66547-09-9 66547-10-2 66584-72-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from Nocardia species, antitumor activity of)

RN 66547-09-9 CAPLUS

CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(1-oxobutyl)- (9CI) (CA INDEX NAME)

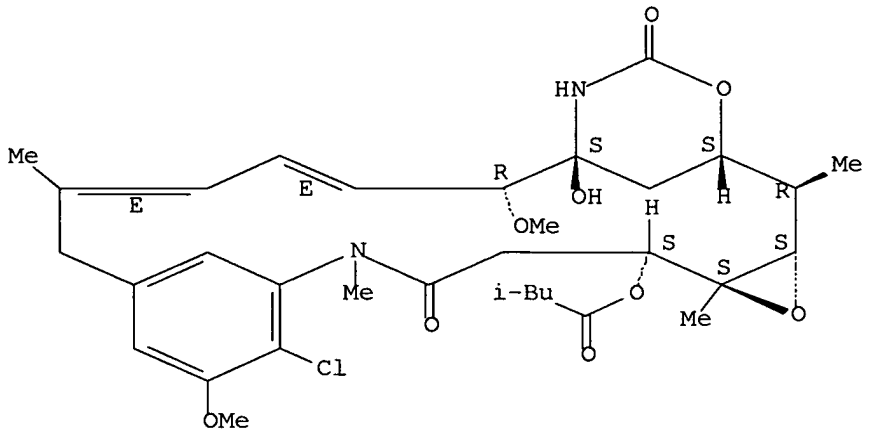
Absolute stereochemistry.
Double bond geometry as shown.



RN 66547-10-2 CAPLUS

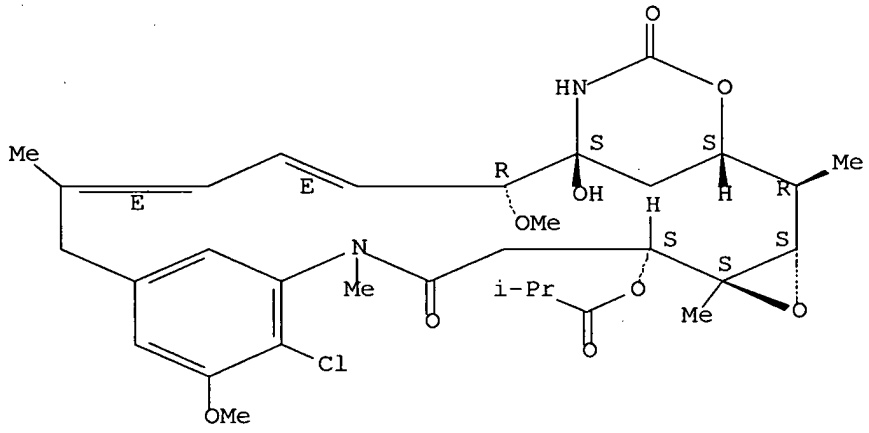
CN Maytansine, O3-de[2-(acetylmethylamino)-1-oxopropyl]-O3-(3-methyl-1-oxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66584-72-3 CAPLUS
CN Maytansine, 2'-de(acetylmethylamino)-2'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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L1            47 S MAYTANSINOL?/CN

     FILE 'CAPLUS' ENTERED AT 16:21:49 ON 17 DEC 2004
L2           110 S L1
L3            16 S L2 AND PURIF?


COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    79.92      93.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -11.20     -11.20

STN INTERNATIONAL LOGOFF AT 16:22:48 ON 17 DEC 2004
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